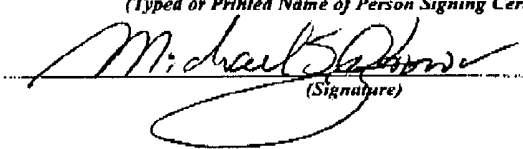


CERTIFICATE OF TRANSMISSION BY FACSIMILE (37 CFR 1.8)			Docket No.
Applicant(s): Dexian DOU et al.			130654-001 (new)
Application No. 09/927,006	Filing Date August 9, 2003	Examiner B. Dell Chism	Group Art Unit 1654
Invention: ANTI-ANGIOGENIC PEPTIDES FOR CANCER TREATMENT			RECEIVED CENTRAL FAX CENTER JUN 24 2004
OFFICIAL			
I hereby certify that this <u> RESPONSE TO RESTRICTION/ELECTION REQUIREMENT </u> <i>(Identify type of correspondence)</i>			
is being facsimile transmitted to the United States Patent and Trademark Office (Fax. No. <u>703-872-9306</u>)			
on <u>June 24, 2004</u> <i>(Date)</i>			
<div style="text-align: center;">Michael S. Gzybowski <i>(Typed or Printed Name of Person Signing Certificate)</i>  <i>(Signature)</i></div>			
Note: Each paper must have its own certificate of mailing.			

RECEIVED
CENTRAL FAX CENTER

JUN 24 2004

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

PATENT APPLICATION

OFFICIAL

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Group
Art Unit: 1654

Attorney
Docket No.:

Applicant: Dexian Dou et al.

Invention: ANTI-ANGIOGENIC PEPTIDES FOR
CANCER TREATMENT

Serial No: 09/927,006

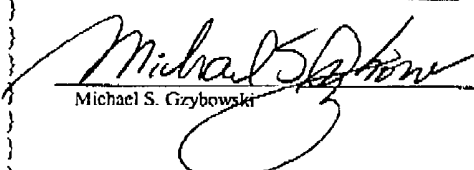
Filed: August 9, 2003

Examiner: B. Dell Chism

Certificate Under 37 CFR 1.8(h)

I hereby certify that this correspondence is being
transmitted to the United States Patent and Trademark
Office via facsimile transmission on the date indicated
below.

on June 24, 2004


Michael S. GzybowskiRESPONSE TO OFFICE COMMUNICATION REGARDING
RESTRICTION/ELECTION REQUIREMENT

Commissioner of Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

In response to the Official Communication mailed May 27, 2004 in connection with the
above-identified application, please amend the application as follows.

Pending Claims are reflected in the listing of the claims which begins on page 2 of this
paper.

Remarks/Arguments begin on page 8 of this paper.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

Pending Claims:

This listing will replace all prior versions, and listings, of claims in the application:

Listing of Claims:

Claim 1 (previously presented): A peptide or its derivative having anti-angiogenic functionality of the structure:

Arg-Asn-Pro-Asp-Gly-Asp-Ile-Asn-Gly-Pro-Tip (hereinafter referred to as {4}),

or

Trp-Pro-Gly-Asn-Ile-Asp-Gly-Asp-Pro-Asn-Arg (hereinafter referred to as {4'}),

or

Tyr-Thr-Met-Asn-Pro-Arg-Lys-Leu-Phe-Asp-Tyr (hereinafter referred to as {5}),

or

Tyr-Asp-Phe-Leu-Lys-Arg-Pro-Asn-Met-Thr-Tyr (hereinafter referred to as {5'}),

or

X-{4}-Y

or

X-{4'}-Y

or

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

X-{5}-Y

or

X-{5'}-Y

or

X-{4}-Ala-{5}-Y

or

X-{4'}-Ala-{5'}-Y

or

X-{5}-Ala-{4}-Y

or

X-{5'}-Ala-{4'}-Y

or

X-{4}-Cys-{5'}-Y

or

X-{4'}-Cys-{5'}-Y

or

X-{5}-Cys-{4}-Y

or

X-{5'}-Cys-{4'}-Y

or

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

$X-\{4\}-(\text{Gly-Gly-Gly-Ser})_n-\{5\}-Y$

or

$X-\{4'\}-(\text{Gly-Gly-Gly-Ser})_n-\{5'\}-Y$

or

$X-\{5\}-(\text{Gly-Gly-Gly-Ser})_n-\{4\}-Y$

or

$\text{Cys}-\{4\}-\text{Ala}-\{5\}-\text{Cys}$

or

$\text{Cys}-\{4'\}-\text{Ala}-\{5'\}-\text{Cys}$

or

$\text{Cys}-\{5\}-\text{Ala}-\{4\}-\text{Cys}$

or

$\text{Cys}-\{5'\}-\text{Ala}-\{4'\}-\text{Cys}$

or

$\text{Ala}-\{4\}-\text{Ala}-\{5\}-\text{Ala}$

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

or

Ala-{4'}-Ala-{5'}-Ala

or

Ala-{5}-Ala-{4}-Ala

or

Ala-{5'}-Ala-{4'}-Ala

wherein the sequence of amino acids is written from the N-terminus (on the left) to the C-terminus (on the right);

wherein X is Acetyl group or other customary N-terminal protecting groups;

wherein y is amine, ethylamine, or other customary C-terminal protecting groups;

wherein n = 1 to 3.

Claim 2 (previously presented): A pharmaceutical composition comprising at least one of said peptides or peptide derivatives of claim 1.

Claim 3 (previously presented): A peptide or its derivative according to claim 1, wherein at least one of amino acids of said peptide or derivative is in a D-form.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

Claim 4 (previously presented): A pharmaceutical composition comprising at least one of said peptides or derivatives of claim 3.

Claim 5 (previously presented): A peptide or its derivative according to claim 1, wherein one amino acid is removed, replaced, or added to said peptide or derivative to form a new molecule.

Claim 6 (previously presented): A pharmaceutical produce comprising at least one of said peptides or derivatives of claim 5.

Claim 7 (previously presented): A peptide or its derivative according to claim 1, wherein either a C-terminal protecting group or an N-terminal protecting group is removed from the peptide or derivative.

Claim 8 (previously presented): A pharmaceutical product comprising at least one of said peptides or derivatives of claim 7.

Claim 9 (original): A method for the treatment of diseases related to angiogenesis by administering to a patient a therapeutic amount of said peptides or its derivatives in claim 1.

Appl. No. 09/927,006

Response. Dated June 24, 2004

Reply to Office Action of May 27, 2004

Claim 10 (original): The method in claim 9 wherein said diseases comprises lung cancer, liver cancer, brain cancer, colon cancer, impairment of vision induced by late-stage diabetes, and other diseases related to angiogenesis.

Claim 11 (original): A method for the treatment of diseases related to angiogenesis by administering to a patient a pharmaceutical composition comprising of said peptides or its derivatives in claim 1.

Claim 12 (original): The method in claim 11 wherein said diseases comprises lung cancer, liver cancer, brain cancer, colon cancer, impairment of vision induced by late-stage diabetes, and other diseases related to angiogenesis.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

•• REMARKS/ ARGUMENTS ••

In the Official Communication of May 27, 2004 the Examiner indicated that applicants' Response of March 18, 2004 was not fully responsive to the Restriction/Election Requirement of March 4, 2004.

In the March 4, 2004 Restriction/Election Requirement the Examiner took the position that claims 1-8 are drawn to a set (SET I) of 16 separate inventions (Groups 1-16) directed to peptides and pharmaceutical products thereof and that claims 9-12 are drawn to a set (SET II) of 16 separate inventions (Groups 17-32) directed to methods of using a peptide pharmaceutical product.

In response to the Restriction/Election Requirement, applicants hereby elect to have Group 1 of SET I examined in the present application.

Notwithstanding this election, applicants request that the Examiner reconsider the Restriction/Election Requirement and examine Group 1 of SET 1 and Group 3 of SET 1 together.

The reason applicants feel that these Groups of SET 1 should be allowed to be examined together is because of their common structural relationship and demonstrated common functionality.

The Examiner is requested to consider that applicants' invention begins with the recognition that of the 38 kringles of Apo(a), only one kringle (the AK38 kringle) was found to have anti-angiogenic activity. In the AK38 kringle, it was determined that the inner ring, which is made from P4 and P5, is primarily responsible for the anti-angiogenic functionality.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

The common anti-angiogenic functionality of P4 and P5 is demonstrated in applicants' Fig. 6. As can be seen in Fig. 6, the anti-angiogenic functionality of P4 and P5 are essentially consistent with one another. P4 corresponds to the first peptide listed in claim 1, i.e. {4} and P5 corresponds to the third peptide listed in claim 1, i.e. {5}.

The common functionality is also related to structural similarities of P4 and P5. Note that as described in applicants' specification in paragraph [0024], applicants discovered that "the active site of AK38 is on the inner ring and P4 and P5 are primarily responsible for the anti-angiogenic effects."

As the Examiner will note from applicants' Fig. 5, the inner ring of the AK38 kringle which is primarily responsible for the anti-angiogenic functionality is made from P4 and P5 and that P4 and P5 extend between a common and shared cysteine units.

This structural relationship of P4 and P5 in the AK38 kringle and the related and demonstrated anti-angiogenic function of the inner ring of the AK38 kringle which is made from P4 and P5 is an important aspect of applicants' invention which is associated to much the same degree to P4 and P5.

On this basis, it is believed to be proper to have similar claims that are directed to P4 and P5 examined in the present application.

Although the Examiner has indicated in the Restriction/Election Requirement that there would be a burden on the Examiner and Patent Office to examine all 32 groups of claims, it would not be such a burden to examine Group 1 of SET 1 and Group 3 of SET 1 together.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

Moreover, the close similarities in functionality of P4 and P5 and the common structural similarities of these peptides as discovered and demonstrated by applicants are believed to justify examining Group 1 of SET 1 and Group 3 of SET 1 together in the present application.

MPEP §803 states:

If the search and examination of an entire application can be made without serious burden, the examiner *must examine* it on the merits, even though it includes claims to independent or distinct inventions.

By proposing to limit the Examiner's search to only P4 and P5 and pharmaceuticals thereof and not electing the remaining 27 peptides, applicants believe that they have greatly reduced the burden on the Examiner to examine Group 1 of SET 1 and Group 3 of SET 1 together in the present application.

37 CFR §1.141 provides that more than one species of an invention can be claimed in a single application provided that the application includes a claim generic to all the claimed species.

MPEP 803.02 states:

If the members of the Markush group are sufficiently few in number or so closely related that a search and examination of the entire claim can be made without serious burden, the examiner *must examine* all claims on the merits, even though they are directed to independent and distinct inventions. In such a case, the examiner will not follow the procedure described below and will not require restriction.

MPEP 803.04 states:

... to further aid the biotechnology industry in protecting its intellectual property without creating an undue burden on the Office, the Commissioner has decided *sua sponte* to partially waive the requirements of 37 CFR§1.141 *et seq.* and permit

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

a reasonable number of such nucleotide sequences to be claimed in a single application. See Examination of Patent Applications Containing Nucleotide Sequences, 1192 O.G. 68 (November 19, 1996).

It has been determined that normally ten sequences constitute a reasonable number for examination purposes. Accordingly, *in most cases, up to ten independent and distinct nucleotide sequences will be examined in a single application without restriction.* In addition to the specifically selected sequences, those sequences which are patentably indistinct from the selected sequences will also be examined. Furthermore, nucleotide sequences encoding the same protein are not considered to be independent and distinct inventions and will continue to be examined together.

Applicants' proposed election to have Group 1 of SET 1 and Group 3 of SET 1 examined in the present application limits the examination of the Markush group of original claim 1 from 27 members to only 2 members. This is believed to conform to a "reasonable number" of peptides in accordance with MPEP 803.04, 37 CFR§1.141 and 1192 O.G. 68 (November 19, 1996).

Favorable reconsideration of the Restriction/Election Requirement by the Examiner and election and examination of Group 1 of SET 1 and Group 3 of SET 1 together in the present application is respectfully requested.


It is believed that the above represents a complete response to the Official Action and reconsideration is requested.

If upon consideration of the above, the Examiner should feel that there remains outstanding issues in the present application that could be resolved, the Examiner is invited to contact applicants' patent counsel at the telephone number given below to discuss such issues.

Appl. No. 09/927,006
Response. Dated June 24, 2004
Reply to Office Action of May 27, 2004

To the extent necessary, a petition for an extension of time under 37 CFR §1.136 is hereby made. Please charge the fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account No. 12-2136 and please credit any excess fees to such deposit account.

Respectfully submitted,


Michael S. Gzybowski
Reg. No. 32,816

BUTZEL LONG
350 South Main Street
Suite 300
Ann Arbor, Michigan 48104
(734) 995-3110

113650.1

-12-